REMARKS

Applicant's counsel thanks the Examiner for the careful consideration given the application.

Amendments

Claims 32 and 47 have been amended to more clearly define over the prior art. In particular the irradiation of skin tissue and the irradiated portion of the skin surface are better distinguished.

Claims 62 and 66 have been amended similarly. Moreover, in response to the Examiner's note that pending claims 62 and 66 do not recite that the fluorescent radiation is received from only a portion of the irradiated skin tissue, claims 62 and 66 have been amended to expressly define that fluorescent radiation is simultaneously received from only a portion of the irradiated portion of the skin surface. The word "simultaneous" is included to express that at an earlier or later stage, for instance before or after having displaced the instrument over the skin, fluorescent radiation may be accumulated from a skin surface area including the entire portion of the skin surface that is irradiated at any one moment. The feature that the surface area from which the radiation is received is larger than 0.1 cm^2 has been removed from claims 62 and 66 and maintained in new dependent claims 73 and 74.

The feature that the surface area from which the radiation is received is larger than 0.1 cm^2 has also been removed from claims 69-72.

Objected claims 49 and 58 have been brought in independent form. Dependent claims 36, 48, 67 and 68 have been amended for consistency with the respective claims from which these claims depend. No new matter has been added.

Claim rejections – 35 USC § 103

Claims 34, 35, 62-68, 73, 74 – Not obvious over Kollias et al. in view of Anderson et al.

Claims 62 and 66 require that the measured fluorescent radiation emitted in response to the irradiation is simultaneously received from only a portion of the irradiated portion of the skin surface.

By simultaneously receiving the measured fluorescent radiation emitted in response to the irradiation from only a portion of the irradiated portion of the skin surface, the irradiation of the skin tissue that emits the fluorescent radiation and accordingly the measured fluorescence are more uniform over the surface from which fluorescent radiation is received. Irradiation and fluorescence intensity along the edges of the irradiated skin surface, are affected relatively strongly by differences in absorption and scattering between different persons. Variations caused by these differences are avoided the more edges of the irradiated portion of the skin surface are outside and spaced from the skin surface portion from which the fluorescent radiation is received. Thus a more precise and better comparable measurement of the AGE content of the skin tissue can be achieved.

According to Kollias et al., the fluorescent radiation is received only from surface portions of the skin surface that are not irradiated.

Use of the same fiber or fibers for delivering and receiving radiation in Kollias et al. would not result in the feature that the measured fluorescent radiation is simultaneously received from only a portion of the irradiated portion of the skin surface. Instead, using the same fiber or fibers for delivering and receiving radiation in Kollias et al. would result in receiving fluorescent radiation from the entire irradiated skin surface, i.e. including areas with more interindividual variations in absorption and scattering.

According to both Kollias et al. and the example of Anderson et al. to which col. 17, l. 55-67 relates (Fig. 6a), the ends of the optical fibers are in contact with the skin. If separate fibers are used for delivering and receiving radiation, as in Kollias et al. and optionally in Anderson et al., the fluorescent radiation is received from portions of the skin surfaces that are not irradiated. If the same fiber or fibers are used for delivering excitation radiation and receiving the fluorescent radiation, the radiation would be delivered and received via the same face or faces of the optical fibers in contact with the skin. Thus, the skin surface from which the fluorescent radiation would be received would be identical to the irradiated skin surface, so the radiation would be received from the entire irradiated skin surface and not from only a portion of the irradiated portion of the skin surface as is required by claims 62 and 66.

With respect to the other (first) example illustrated by Figs. 1 and 2, Anderson et al. it is observed that it would not have been obvious to consider that example, because the camera with a lens and a CCD is specifically used for identifying local anomalies of the skin. Moreover, also in this example Anderson et al. teaches that the fluorescent radiation is received from the entire irradiated portion of the skin surface. According to Anderson et al., col. 11, l. 45-47:

> *"A lens 50 is positioned to couple only fluorescence and reflectance from the area of skin coincident with treatment beam 40 into fiber 48."*

This confirms the teaching to receive the fluorescent radiation from the entire irradiated portion of the skin surface.

Thus, the combination of Kollias et al. and Anderson et al. would not have resulted in simultaneously receiving fluorescent radiation from only a portion of the irradiated portion of the skin surface.

Moreover, it would not have been obvious to add the feature that the measured fluorescent radiation is received from only a portion of the irradiated portion of the skin surface to the combination of Kollias et al. and Anderson et al., because this feature entails that, in relation to the amount of light irradiated onto the skin, less fluorescence would be received than when the fluorescent radiation would have been received from the entire irradiated portion of the skin surface. Absent the insight that influences of differences in scattering and absorption between subjects have a relatively important influence along the edges of the irradiated portion of the skin surface, it would not have been obvious to include special measure that result in receiving less fluorescence than is technically possible.

Claims 32, 33, 33-40, 43-45, 47, 48, 54-57, 60, 61 – Not obvious over Kollias et al.

Claims 32 and 47 require that the measured autofluorescence is received from an irradiated portion of the skin surface of at least 1 cm^2.

By receiving the fluorescent radiation from an irradiated portion of the skin surface of at least 1 cm^2, the fluorescence is received from a relatively large surface area of the skin that is directly irradiated. By measuring over a relatively large surface, the likelihood and magnitude of

disturbances of the measurement result due to local variations in skin properties is reduced. Moreover, measuring radiation from a large irradiated surface is also advantageous because variations in irradiation and fluorescence intensity, including scattered irradiation and fluorescence along edges, which are affected by differences in absorption and scattering between different persons, are relatively smaller for a large surface than for a small surface. Thus a more precise and better comparable measurement of the AGE content of the skin tissue can be achieved.

Firstly, as observed above, according to Kollias et al., the fluorescent radiation is received only from surface portions of the skin that are not (directly) irradiated. As can be seen in Figs. 10A and 10B, separate light guides having ends adjacent the skin are arranged next to each other and are coupled for emitting and, respectively, receiving light from the skin so that the radiation is received from another surface portion of the skin than the surface portion of the skin that is irradiated. Regarding the light guides, it is disclosed that these may be flexible fiber optic bundles (see col. 1, l. 10, col. 7, l. 2-3). It is also disclosed that the radiation source may comprise a flexible fiber optic arm that comprises a glass or quartz fiber (col. 5, l. 52-56). Clearly a glass or quartz fiber optic can only be flexible if it is very thin. To be feasible for transporting a useful amount of light, the glass or quartz fiber optic must inherently be part of a bundle.

In the previous Office action, it was said that Kollias et al. inherently discloses details of a radiation delivery optical assembly capable of irradiating a skin surface and capable of being used as the radiation pick-up optical fiber. However, using the same fibers for irradiating a skin surface and picking-up radiation from the skin requires excitation radiation and received fluorescence to be subdivided. This requires a two-way coupler, for instance of a type in which emitted light and received light are directed via different portions of an angular range in front of the end face of the fiber bundle via which light can be coupled into or out of the fiber bundle (see for instance U.S. Patent 4,773,722) or of a type in which radiation is selectively reflected by semi-reflective mirrors. Since such devices complicate the design, attenuate light and constitute a likely source of noise and other artefacts, it would not have been obvious to opt for a modification of Kollias et al. involving two-way coupling of light through fibers of an optical fiber bundle. The undesirable side effects of such a solution are of particular relevance since light has to be dosed and measured via the optical fibers with high quantitative accuracy and not merely serves for transmitting digital data (which only requires that two values can be distinguished).

In view of these considerations, it would not have been obvious for the skilled person to provide two-way light transmission via fibers of a fiber optic bundle in a method and apparatus as disclosed by Kollias et al. Therefore, receiving fluorescent radiation from an irradiated portion of the skin surface by using the same optical fibers for emitting and receiving light would not have been obvious in view of Kollias at al.

Furthermore, while in col. 14, l. 15-18 and col. 15, l. 45-46, Kollias et al. discloses directing the light to the skin surface via reflective optics, such as a prism, or directly through the air, as alternatives to directing the light via optical fibers, no alternative is disclosed for the pick-up optical fibre bundle held closely to or against the skin surface. In the position close to or against the skin, the light receiving fiber bundle obscures the skin surface from irradiation directed via a reflective optic or directly through the air. Accordingly, even if the excitation irradiation would be directed via reflective optics, such as a prism, or directly through the air, the fluorescent radiation received via the light receiving fiber bundle would still not have been received from an irradiated portion of the skin surface.

Thus, even if one of the alternatives for directing the irradiation to the skin as disclosed by Kollias et al. would have been applied, the fluorescence would still not have been received from an irradiated portion of the skin.

Thus, it would not have been obvious in view of Kollias et al. to provide for receiving the fluorescence from an irradiated portion of the skin surface, irrespective whether the light is directed to the skin surface via an optical fiber bundle or via one of the alternatives.

It was also said in the previous office action that it would have been well within the skill of the art to implement a radiation pick-up optical fiber capable of receiving measured fluorescent radiation from a skin surface having at least the same size or a larger size than the size of the skin surface irradiated.

However, according to amended claims 32 and 47, the surface area of the irradiated portion of the skin surface must inherently be at least 1 cm^2, otherwise the fluorescent radiation could not be received from an irradiated surface area of at least 1 cm^2. According to Kollias et al. col. 5, l.

57-58, "The portion of the skin irradiated may be less than about 1 square cm, and more preferably is about 0.2 square cm.". The range "less than about 1 square cm" does not unambiguously include the value 1 square cm, because that disclosed range ends where the range "about one square cm" begins. This in contrast with for example a range defined as "about one square cm or less", which would unambiguously have included the "about one square cm" range. That the range taught by Kollias et al. ends short of 1 cm^2 is also supported by the preferred value of 0.2 cm^2 which is well remote from the 1 cm^2 value. In view of that preferred value, when proposing a modification to Kollias et al. involving the measurement of fluorescence received from an irradiated portion of the skin, it would at least not have been obvious to provide that the surface area of the portion of the irradiated portion of the skin surface from which the fluorescence is received is at least 1 cm^2.

Thus, since it would not have been obvious over Kollias et al. to provide that the fluorescence is received from a surface area of the irradiated surface portion of the skin larger than 1 cm^2, the method according to claim 32 and the apparatus according to claim 47 are not obvious over Kollias et al.

For all the foregoing reasons, it is believed that all of the claims now present in this application are in condition for allowance, which is respectfully requested. If any further fees are required by this communication, please charge such fees to our Deposit Account No. 16-0820, Order No. VOB-34537US1.

Respectfully submitted,
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Date: 4-22-10